

CLAIMS

We claim:

- 5 1. A purified nucleic acid comprising a sequence at least 80% identical to SEQ ID NO:15, wherein said sequence encodes IL-32, and wherein said sequence comprises exon 3 and exon 4 of IL-32 in substantially contiguous association.
- 10 2. The nucleic acid of Claim 1, wherein said IL-32 is an alpha isoform comprising the amino acid sequence set forth as SEQ ID NO:7.
- 15 3. The nucleic acid of Claim 1, wherein said IL-32 is a beta isoform comprising the amino acid sequence set forth as SEQ ID NO:8.
4. The nucleic acid of Claim 1, wherein said IL-32 is a delta isoform comprising the amino acid sequence set forth as SEQ ID NO:10.
5. The nucleic acid of Claim 1, wherein said sequence lacks intron 4 of IL-32.
- 20 6. The nucleic acid of Claim 1, wherein said sequence is at least 90% identical to SEQ ID NO:15.
7. The nucleic acid of Claim 1, wherein said sequence is selected from the group consisting of SEQ ID NO:3, SEQ ID NO:4 and SEQ ID NO:6.
- 25 8. The nucleic acid of Claim 1, wherein said sequence is operably linked to a heterologous promoter.
9. The nucleic acid of Claim 8, wherein said nucleic acid is contained within a vector.
- 30 10. A host cell comprising the vector of Claim 9.
11. A purified protein encoded by the nucleic acid of Claim 1.

12. The protein of Claim 11, wherein said IL-32 is an alpha isoform comprising the amino acid sequence set forth as SEQ ID NO:7.

13. The protein of Claim 11, wherein said IL-32 is a beta isoform comprising the amino 5 acid sequence set forth as SEQ ID NO:8.

14. The protein of Claim 11, wherein said IL-32 is a delta isoform comprising the amino acid sequence set forth as SEQ ID NO:10.

10 15. The protein of Claim 11, wherein said IL-32 is not a gamma isoform.

16. The protein of Claim 11, wherein said IL-32 does not comprise the amino acid sequence set forth as SEQ ID NO:14.

15 17. The protein of Claim 11, wherein said IL-32 is a recombinant protein expressed in a cell selected from the group consisting of a bacterial cell, a yeast cell, an insect cell, and a mammalian cell.

18. The protein of Claim 17, wherein said recombinant protein is a fusion protein.

20 19. An antibody, which binds to the protein of Claim 11.

20. The antibody of Claim 19, wherein said antibody is a monoclonal antibody.

25 21. An Fab fragment of the monoclonal antibody of Claim 20.

22. The monoclonal antibody of Claim 20, wherein said monoclonal antibody is chosen from 32-4 and 32-9.

30 23. The monoclonal antibody of Claim 20, wherein said monoclonal antibody is a humanized monoclonal antibody.

24. The monoclonal antibody of Claim 20, wherein said monoclonal antibody inhibits IL-32-induced TNF α production by a target cell.

25. The monoclonal antibody of Claim 20, wherein said monoclonal antibody inhibits IL-32-induced I_KB degradation in a target cell.

5 26. The monoclonal antibody of Claim 20, wherein said monoclonal antibody inhibits rapid IL-32-induced p38 MAPK phosphorylation in a target cell.

27. A method for inducing TNF α production, comprising contacting at least one cell with an IL-32 protein under conditions suitable for inducing TNF α production.

10 28. The method of Claim 27, wherein said IL-32 protein is selected from the group consisting of an alpha isoform, a beta isoform, a gamma isoform and a delta isoform.

29. The method of Claim 27, wherein said at least one cell comprises a leukocyte.

15 30. The method of Claim 29, wherein said leukocyte is selected from the group consisting of monocytes and macrophages.

31. A method of treating a subject, comprising:

20 a) providing a subject and an antibody that binds to IL-32; and
b) administering said antibody to said subject.

32. The method of Claim 31, wherein said IL-32 is selected from the group consisting of an alpha isoform, a beta isoform, a gamma isoform and a delta isoform.

25 33. The method of Claim 31, wherein said subject has, is suspected of having, or is at risk of having an autoimmune disease.

34. The method of Claim 33, wherein said autoimmune disease is selected from the group consisting of multiple sclerosis, myasthenia gravis, autoimmune neuropathy, autoimmune uveitis, Crohn's disease, ulcerative colitis, primary biliary cirrhosis, autoimmune hepatitis, autoimmune hemolytic anemia, pernicious anemia, autoimmune 5 thrombocytopenia, type 1 diabetes mellitus, Grave's disease, Hashimoto's thyroiditis, autoimmune oophoritis and orchitis, temporal arteritis, anti-phospholipid syndrome, Vasculitides, Behcet's disease, rheumatoid arthritis, systemic lupus erythematosus, scleroderma, polymyositis, dermatomyositis, spondyloarthropathy, Sjogren's syndrome, psoriasis, dermatitis herpetiformis, pemphigus vulgaris, and vitiligo.

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35. The method of Claim 31, wherein said antibody is selected from the group consisting of a human monoclonal antibody and a humanized mouse monoclonal antibody.

36. The method of Claim 33, wherein said administering is done under conditions 15 suitable for alleviating at least one symptom of an autoimmune disease.

37. The method of Claim 31, wherein said subject is a sepsis patient.

38. A method for screening for inhibitors of IL-32, comprising:

20 a) providing the IL-32 protein of Claim 11, and at least one drug candidate; and
b) analyzing the effect of said drug candidate on at least one activity of said IL-
32 protein.

39. The method of Claim 38, wherein said IL-32 is a recombinant protein selected from 25 the group consisting of an alpha isoform, a beta isoform, a gamma isoform and a delta isoform.

40. The method of Claim 38, wherein said drug candidate is selected from the group 30 consisting of a IL-32-reactive monoclonal antibody, and a dominant-negative IL-32 variant.

41. The method of Claim 38, wherein at least one activity of said IL-32 protein comprises upregulation of TNF α expression.

42. A method of treating a subject, comprising:

- a) providing a subject and the IL-32 protein of Claim 11; and
- b) administering said IL-32 protein to said subject.

5 43. The method of Claim 42, wherein said IL-32 is a recombinant protein selected from the group consisting of an alpha isoform, a beta isoform, a gamma isoform and a delta isoform.

10 44. The method of Claim 42, wherein said subject has, is suspected of having, or is at risk of having cancer.